

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

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## FILE COPY 206

### INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

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Applicant's or agent's file reference 257/245WO	Date of Mailing (day/month/year)
International application No. PCT/US02/02600	International filing date (day/month/year) 28 JANUARY 2002
Applicant NANOGEN	

1. This International Searching Authority

- (i) considers that there are 21 (number of) inventions claimed in the international application covered by the claims indicated below/on an extra sheet:  
Please See Extra Sheet.

and it considers that **the international application does not comply with the requirements of unity of invention** (Rules 13.1, 13.2 and 13.3) for the reasons indicated below/on an extra sheet:  
Please See Extra Sheet.

- (ii) ☐ has carried out a partial international search (see Annex) ☒ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:  
1-2, 6-15, 17-40
- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid.

2. The applicant is hereby **invited**, within the time limit indicated above, to pay the amount indicated below:

\$ 210.00	X	20	=	\$ 4200.00
Fee additional per invention		number of additional inventions		total amount of additional fees

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest**, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☐ Claim(s) Nos. \_\_\_\_\_ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

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International application No.  
PCT/US02/02600

I. This International Search Authority has found 21 inventions claimed in the International Application covered by the claims indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

- I. Claims 1-2,6-15 , 17-40, drawn to a water-soluble pegylated kinase substrate.
- II. Claims 1, 3, 5-15, 17-40, drawn to a water-soluble pegylated phosphatase substrate.
- III. Claims 1, 4, 6-15, 17-40, drawn to a water-soluble pegylated protease substrate.
- IV. Claims 1-2, 6-14,16-19, 21-40, drawn to a water-soluble saccharide modified kinase substrate.
- V. Claims 1, 3, 5-14,16-19, 21-40, drawn to a water-soluble saccharide modified phosphatase substrate.
- VI. Claims 1, 4, 6-14, 16-19, 21-40, drawn to a water-soluble saccharide protease recognition substrate.
- VII. Claims 41, 43-52, 54-77 drawn to a library of water-soluble pegylated kinase substrate.
- VIII. Claims 41, 42-52, 54-77 drawn to a library of water-soluble pegylated phosphatase substrate.
- IX. Claims 41, 43-52, 54-77, drawn to a library of water-soluble pegylated protease substrate.
- X. Claims, 41, 43-51, 53-56, 58-77, drawn to library of water-soluble saccharide modified kinase substrate.
- XI. Claims 41, 42-51, 53- 56, 58-77, drawn to library of water-soluble saccharide modified phosphatase substrate.
- XII. Claims 41, 43-51, 53-56, 58-77, drawn to a library of water-soluble saccharide protease substrate.
- XIII. Claims 78, 79, 82-91, drawn to a method of screening a library of water-soluble pegylated kinase substrate.
- XIV. Claims 78, 80, 82-91, drawn to a method of screening a library of water-soluble pegylated phosphatase substrate.
- XV. Claims 78, 81, 82-91, drawn to a method of screening a library of water-soluble pegylated protease substrate.
- XVI. Claims 78, 79, 82-91, drawn to a method of screening a library of water-soluble saccharide modified kinase substrate.
- XVII. Claims 78, 80, 82-91, drawn to a method of screening a library of water-soluble saccharide modified phosphatase substrate.
- XVIII. Claims 78, 81, 82-91, drawn to a method of screening a library of water-soluble saccharide protease substrate.
- XIX. Claims 92-95, 97-105, drawn to a protein kinase assay of water-soluble peptide substrates substrate.
- XX. Claims 92-94, 96-105, drawn to a phosphatase assay of water-soluble peptide substrates.
- XXI Claims 106-113, drawn to a protease assay of water soluble peptide substrates.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

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The inventions listed as Groups I-XXI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

In the present case, making one or more (e.g. plurality) labeled water solubilizing peptides utilizing water solubilizing agents such as PEG and labels including radiological labels is already known in the prior art (see e.g. US Pat. No. 5,622,685 at col. 2-4; and US Pat. No. 5,891,418 at col.1-2; col. 38, Example 16). Accordingly, unity of invention cannot be predicated on the labeled water-soluble peptides as being a special technical feature. Additionally, it is noted that the formula presented for the water-soluble peptidic substrates does not constitute a proper "Markush group" of compounds. A proper Markush claim can only be acknowledged if it can be shown that:

- I) all alternatives have a common activity; AND
- II) an inventive, common structural element.

In the present instance, the formula of claim 1 (and other independent claims) lacks a common structural element since there is virtually no fixed structural element which may be regarded as representing the inventive structural element; and since labeled water solubilized peptide substrates are already known in the art; the Markush an "inventive" common structural element. Additionally, all of the alternatives do not possess a "common activity" since the peptide portion may represent different patentably distinct peptide compounds usable as substrates from different enzymes. Accordingly, compound claims and methods of use thereof contain patentably distinct compounds including those containing different enzyme substrates (e.g. phosphatases/kinases/proteases) and solubilizing agents (e.g. PEG and polysaccharides). Libraries of compounds are patentably distinct over individual compounds, since a special technical feature of a plurality of compounds, unlike a single compound, may reside in the patentability of the combination. Additionally, methods of screening different enzymes (e.g. proteases/kinases/phosphatases) are patentably distinct methods due to differences in method objective, use of patentably distinct substrates and the use of different reagents and reaction conditions.